REMARKS

I. Status of Claims

Claims 1-22 are pending in this application. Claims 1-22 are rejected. Applicants thank the Examiner for stating that claim 18 contains allowable subject matter.

Claims 1 and 19 have been amended to more particularly point out Applicants' invention. Claim 17 has been amended to depend from claim 16.

II. Elections/Restrictions

Applicants understand that the restriction requirement is made final but respectfully request that the Examiner reconsider the requirement. Applicants assert that it is within the scope and spirit of claim 1 to describe and claim an analyte detection method that utilizes more than one measurement method. It is within this spirit that the USPTO has time and again allowed claims in the same application that are directed to the synthesis of a single product via more than one synthetic pathway.

Accordingly, Applicants respectfully request that the subject matter of claim 1 directed to determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal be re-considered in the event the Examiner finds the rest of claim 1 allowable.

Regarding claims 23-31 which have been withdrawn from consideration by the Examiner, Applicants thank the Examiner for indicating that rejoinder of these kit claims will be considered by the Examiner in the event that the method claims are found allowable.

III. Information Disclosure Statement

The Examiner has stated that the information disclosure statement filed April 3, 2003, fails to comply with 37 CFR 1.98(a)(2) which requires a copy of each cited foreign patent and each non-patent literature publication. Office Action, p. 3. Applicants respectfully point out to the Examiner that the USPTO acknowledged receipt of PTO-1449 form and the 31 documents cited therein on April 3, 2002, as indicated on the enclosed copy of the postcard receipt. Applicants respectfully submit that all requirements of 37 CFR 1.98(a)(2) have been fulfilled.

IV. Priority

The Examiner has stated that Applicants have not filed a certified copy of the priority application as required by 35 U.S.C. 119(b). Applicants respectfully point out to the Examiner that the USPTO acknowledged receipt of the certified copy of the priority application on December 21, 2001, as indicated on the enclosed copy of the postcard receipt.

V. Rejection under 35 U.S.C. § 112, Second Paragraph

1. Rejection at paragraph (6)

The Examiner has rejected claims 1-17 and 18-22 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicants regard as the invention. Specifically, the Examiner states that the term "associated" is vague because "it is unclear as to whether these reagents are bound to the solid phase and labels or if they are just associated by incubation of

reagents." Office Action at page 4. Applicants respectfully point out to the Examiner that the term "associated" is clearly defined in the specification at paragraph 35. According to the specification, the term "associated" encompasses, for example, "a covalent and a noncovalent bond, a direct and an indirect linkage, adsorption to a surface and inclusion in a recess or a cavity, etc." Further, numerous examples are given to demonstrate the meaning of the term "associated." Specification of pending application at paragraph 35. Thus, the term "associated" encompasses reagents being bound to the solid phase and label, and also association by incubation of reagents. If Applicants have not addressed the Examiner's rejection to the Examiner's satisfaction, Applicants request clarification of the rejection. Otherwise, Applicants respectfully request that this rejection be withdrawn.

2. Rejection at paragraph (7)

The Examiner has rejected claims 1 and 19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicants regard as the invention. Specifically, the Examiner states that the recitation that the saturation of R2 takes place "at a higher analyte A concentration, at a later time in the incubation, or at a higher analyte A concentration and at a later time in the incubation" is redundant. Office Action at page 4. Applicants respectfully disagree. One skilled in the art would understand that saturation takes place at any one of the events listed in the claims. However, in order to further prosecution, Applicants have amended claims 1 and 19 so that it is clear that saturation may occur at any one of

three events (a), (b), or (c) as now listed in the amended claims. Applicants request that this rejection be withdrawn.

3. Rejection at paragraph (8)

The Examiner has rejected claims 5, 6 and 19 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicants regard as the invention. Specifically, the Examiner states that the binding relationships of R3, X, L2, and Y are unclear. Applicants respectfully disagree. In claims 5, 6, and 19, R3 is associated with a member X of a specific binding pair. L2 is associated with a binding pair member Y. One skilled in the art would understand that R3 is associated with X and L2 is associated with Y. One skilled in the art would further understand that X and Y are members of a specific binding pair. The specification states that "[t]he members of a specific binding pair are two molecules which in each case possess at least one structure which is complimentary to a structure possessed by the other molecule, with two molecules being able to bind to each other by means of the complementary structures binding to each other." Specification at paragraph 28. Thus, one skilled in the art would understand that during incubation, specific binding pair partners X and Y are able to bind to each other. Applicants assert that the language is clear in the claims, and respectfully request that this rejection be withdrawn.

4. Rejection at paragraph (9)

The Examiner has rejected claim 17 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicants regard as the invention. Specifically, the Examiner states that the interaction of claim 1

comprising an energy transfer is vague because "it is unclear from which reactants this energy transfer is directed from." Office Action at page 4. Applicants respectfully disagree with this rejection. Claim 16 reads as follows:

> 16. The method of claim 1, wherein, as a consequence of formation of a sandwich, components of a signal-forming system, which include at least one of L1 and L2, are brought to a distance from each other which permits an interaction between these components, and the extent of the interaction is measured.

Claim 17, as now amended, reads:

> 17. The method of claim 16, wherein the interaction comprises an energy transfer.

Thus, according to claim 16, components of a signal-forming system which include at least one of L1 and L2 are brought to a distance from each other which permits an interaction between the components. According to the specification, "a 'signal-forming system' can have one or more components, with at least one component being a detectable label. A label is to be understood as being any molecule which itself produces a signal or which is able to induce the production of a signal . . . ." Specification at paragraph 36. The specification further states that "[a] signal-forming system can also encompass components which, being in spatial proximity to each other, can enter into a detectable interaction, for example in the form of energy donors and energy recipients . . . ." Specification at paragraph 40. Thus, one skilled in the art would understand after reading the specification and claims 16 and 17, that the interaction, or for example, energy transfer, can take place between the components of the signal-forming system wherein one of the components is a label, and further understand that the determination of which component is the energy donor and which

component is the energy recipient depends entirely on the selection of components and each component's ability to donate or receive energy. Applicants respectfully request that this rejection be withdrawn.

5. Rejection at paragraph (10)

The Examiner has rejected claim 8 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicants regard as the invention. Specifically, the Examiner states that the recitation that R1, R2 and R3 can be the same binding partner is confusing. Applicants respectfully disagree. According to the specification, to say that R1, R2, and R3 can be the same binding partner, means that each entity is a binding partner of an analyte, wherein all three entities recognize the same binding site of the analyte. See e.g., specification at paragraphs 16, 17. This is not to say that R1, R2, and R3 are the same binding entity. As illustrated in paragraph 16 where binding partners such as R2 and R3 can be the same, the specification states that when this is the case, in an embodiment, R2 is employed in the form of R2 aggregates and/or many R2 molecules which are associated with a suspendable solid phase, whereas R3 is employed as a solitary molecule, at least in the initial phase of the incubation. Id. Thus, R1, R2, and R3 can each take on a different form but each entity will recognize the same binding site of the analyte. Applicants respectfully request that this rejection be withdrawn.

VI. Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1-4, 7-12 and 16 under 35 U.S.C § 102(b) as being anticipated by Cragle et al, U.S. Patent No. 4,595,661 ("the '661 patent").

Applicants' claim 1, as amended, reads as follows:

> 1. A method for detecting an analyte A in a sample, comprising:
>
> incubating an incubation mixture comprising a sample with an analyte A-specific binding partner R1, which is associated with a solid phase, an analyte A-specific binding partner R2, which is associated with a label L1, and an analyte A-specific binding partner R3, which is associated with a label L2, wherein saturation of analyte A-binding sites of the binding partner R2 takes place at a) a higher analyte A concentration, b) at a later time in the incubation, or c) at a higher analyte A concentration and at a later time in the incubation, than does saturation of analyte A-binding sites of the binding partner R3; and
>
> determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal.

The Examiner states that the '661 patent teaches that a fluid sample containing an antigenic substance (Ag) is contacted with L-Ab_a (a labeled antibody) which allegedly corresponds to Applicants' R2 associated with L1, and Ab_b-SC (an antibody bound to a solid carrier) which allegedly corresponds to Applicants' R1 associated with a solid support to form the complex L-Ab_a-Ag-Ab_b-SC. The Examiner also states that after formation of this complex, the unreacted L-Ab_a is measured, followed by the addition of L-Ab_c (a different labeled antibody) which allegedly corresponds to Applicants' R3 associated with a label L2 and is present in the amount to avoid the hook effect. Office Action at page 5. The Examiner states that the '661 patent teaches that L-Ab_c has a constant K that is lower than the K of L-Ab_a. Office Action at page 5. From this, the Examiner concludes that the saturation of L-Ab_a would take place at a higher analyte A

concentration than that of L-Ab_c. Office Action at page 6. The Examiner relies on this conclusion as the basis for a 102(b) rejection, asserting that L-Ab_a and L-Ab_c are the same as Applicants' R2-L1 and R3-L2, respectively, and just like the relationship between R2-L1 and R3-L2, saturation of L-Ab_a takes place at a higher analyte concentration than L-Ab. No other limitations of claim 1 are addressed.

For the reasons discussed below, Applicants traverse this rejection and respectfully disagree with the Examiner's assertions regarding the '661 patent.

First, Applicants respectfully point out that the entity L-Ab_c is contacted with the fluid at the same time that the other entities L-Ab_a and Ab_b-SC are contacted with the fluid, and not after the measurement of L-Ab_a. See the '661 patent, col. 2, line 67 - col. 3, line 6, and claim 1.

Second, Applicants respectfully assert that the Examiner's conclusion that the saturation of L-Ab_a in the '661 patent occurs at a higher analyte A concentration than that of L-Ab_c is erroneous. The '661 patent teaches that L-Ab_a has a higher affinity constant than L-Ab_c. See e.g., '661 patent, col. 3, lines 34-36. It is known to those skilled in the art that the higher the affinity of an antibody for an antigen, i.e. the higher the affinity constant, then the lower the concentration of antigen is necessary for 50% of antigen to bind to the antibody. Thus, in the '661 patent, saturation of L-Ab_a would take place at a lower concentration of antigen, than its counterpart, L-Ab_c, contrary to the Examiner's contention that the saturation of L-Ab_a takes place at a higher concentration of the antigen.

Moreover, the Examiner has not shown that the '661 patent anticipates each and every element of Applicants' claims. See M.P.E.P. § 2131. For instance, as discussed

above, the Examiner has made certain incorrect assertions about the '661 patent and how it allegedly relates to Applicants' claims in terms of saturation of an antibody at higher analyte-A concentrations. The Examiner fails to discuss how the '661 patent anticipates Applicants' claim limitation regarding saturation of R2 occurring at either 1) a later time or 2) at a higher concentration of analyte A and at a later time, versus R3. Note that one cannot know the speed of a reaction based on its equilibrium constant K. Thus, the '661 patent does not provide information regarding the kinetics of the binding of an antigen to an antibody.

In addition, the Examiner fails to show how the '661 patent anticipates the measurement limitations claimed in Applicants' claims. The '661 patent teaches that a *single measurement* is taken of bound L-Ab_a. Applicants claim the taking of at least two measurements of, for example, two different bound labeled antibodies. Specifically, Applicants' claims, as amended, teach determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal. Thus, the '661 patent does not teach or anticipate the measurement methods taught by Applicants' claims.

Accordingly, Applicants respectfully contend that the '661 patent does not anticipate Applicants' claims and ask that this rejection be withdrawn.

VII. Rejections under 35 U.S.C § 103

The Examiner has rejected dependent claims 5, 6, 13-15, 17, and 19-22, under 35 U.S.C. § 103 in view of certain art.

A. The '661 patent in view of Cragle et at, U.S. Patent No. 4,590,169

The Examiner has rejected dependent claims 13-15 under 35 U.S.C. § 103 as being unpatentable over the '661 patent in view of Cragle et at, U.S. Patent No. 4,590,169 ("the '169 patent"). Due to the dependency of claims 13-15, the limitations of claim 1 must be read into claims 13-15 when determining the alleged obviousness of claims 13-15. Accordingly, Applicants respond below.

Applicants traverse this rejection. For the reasons discussed above, the '661 patent does not anticipate Applicants' claim 1. For instance, the '661 patent does not teach or make obvious Applicants' claim limitation regarding saturation of R2 occurring either 1) at a later time or 2) at a higher concentration of analyte A and at a later time, versus R3. Nor does the '661 patent teach or make obvious the claim limitations of determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal. For these same reasons, the '661 patent does not suggest or make obvious Applicants' claims 13-15.

Contrary to the Examiner's assertions, the deficiencies of the '661 patent which fail to teach or make obvious Applicants' invention cannot be found within the four corners of the '169 patent. The '169 patent is directed to a direct particle agglutination assay for an antigenic substance which comprises contacting a fluid with an antibody (Ab) coated particle (P). The fluid is also contacted with a second antibody (Ab_a) coated particle (P_1). The Examiner cites the '169 patent solely for allegedly disclosing a suspendable solid phase. The '169 patent, however, does not teach or even suggest any of the claim limitations of claim 1. Since the '661 patent, as demonstrated above,

does not teach or make obvious Applicants' claims, the attempt to combine it with the '169 patent fails to render Applicants' claims 1 and 13-15 obvious. Applicants respectfully request that this rejection be withdrawn.

B. The '661 patent in view of Marquardt et al, U.S. Patent No. 6, 610,494

The Examiner has rejected dependent claims 5 and 6, independent claim 19, and its dependent claims 20-22 under 35 U.S.C. § 103 as being unpatentable over the '661 patent in view of Marquardt et al, U.S. Patent No. 6,610,494 ("Marquardt"). Due to the dependency of claims 5-6, the limitations of claim 1 must be read into claims 5-6 when determining the alleged obviousness of claims 5-6. Accordingly, Applicants respond below.

For reasons discussed above, the '661 patent fails to teach or make obvious Applicants' claim 1. For instance, the '661 patent does not teach or make obvious Applicants' claim limitation regarding saturation of R2 occurring either 1) at a later time or 2) at a higher concentration of analyte A and at a later time, versus R3. Nor does the '661 patent teach or make obvious the measurement methods of claim 1. For these same reasons, the '661 patent does not suggest or make obvious the more narrow limitations of Applicants' claims 5-6.

With regard to the Examiner's contention that the '661 patent teaches the taking of two different measurements (Office Action, p. 8), Applicants respectfully disagree. As discussed above and as made evident in at least claim 1 of the '661 patent, the entity L-Ab_c is added at the same time as the other entities, followed by incubation, and the taking of a single measurement of L-Ab_a. There is no indication, even in the examples

of the '661 patent, that measurements are taken of, for example, two different bound labeled antibodies, as claimed in claim 1 of Applicants' claims.

Contrary to the Examiner's assertions, the deficiencies of the '661 patent which fail to teach or make obvious Applicants' invention cannot be found within the four corners of Marquardt. Marquardt is directed to a method of detecting via a solid-phase assay the amount of biological activity and/or the quantity of a biologically active substance. See e.g., Marquardt, col. 2, lines 61-65. The Examiner cites Marquardt solely for allegedly disclosing an XY binding pair. Marquardt, however, does not teach the limitations of claim 1 as claimed in Applicants' claims. For these same reasons, Marquardt does not suggest or make obvious the more narrow limitations of Applicants' claims 5-6. Since the '661 patent, as demonstrated above, does not teach or make obvious Applicants' claims, the attempt to combine it with Marquardt fails to render Applicants' claims 1 and 5-6 obvious. Applicants respectfully request that this rejection be withdrawn.

For the same reasons as discussed above, the '661 patent does not teach or make obvious Applicants' independent claim 19 and dependent claims 20-22. For instance, the '661 patent does not teach a binding partner R3 associated with a member X of a specific binding pair. Nor does the '661 patent teach or make obvious the measurement methods of claim 19. Furthermore, Marquardt's alleged disclosure of an XY binding pair fails to teach or even suggest any of the other limitations as claimed in claim 19. Thus, the '661 patent in view of Marquardt does not render Applicants' claim 19 obvious. Nor do these references make obvious the more narrow limitations of claims 20-22. Applicants respectfully request that this rejection be withdrawn.

C. The '661 patent in view of Pitner et al, U.S. Patent No. 5,641,629

The Examiner has rejected dependent claim 17 under 35 U.S.C. § 103 as being unpatentable over the '661 patent in view of Pitner et al, U.S. Patent No. 5,641,629 ("Pitner"). Due to the dependency of claim 17, the limitations of claims 1 and 16 must be read into claim 17 when determining the alleged obviousness of claim 17. Accordingly, Applicants respond below.

For reasons discussed above, the '661 patent does not teach or even suggest Applicants' claimed invention. For instance, the '661 patent does not teach the limitations of claim 1 regarding saturation of R2 occurring either 1) at a later time or 2) at a higher concentration of analyte A and at a later time, versus R3. Nor does the '661 patent teach or make obvious the measurement methods claimed in claim 1. For these same reasons, the '661 patent does not suggest or make obvious the more narrow limitations of dependent claim 17.

Contrary to the Examiner's assertions, the deficiencies of the '661 patent which fail to teach or make obvious Applicants' invention cannot be found within the four corners of Pitner. The Examiner cites the Pitner solely for allegedly disclosing energy transfer techniques. Pitner, however, cannot cure the deficiencies of the '661 patent. Since the '661 patent, as demonstrated above, does not teach or make obvious Applicants' claims, the attempt to combine it with Pitner fails to render Applicants' claims 1 and 17 obvious. Applicants respectfully request that this rejection be withdrawn.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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Dated: October 31, 2005

By: Carol P. Einaudi
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CPE-SJH-USN

PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

New U.S. Application for:
DETECTION METHODS

Inventors: Carsten SCHELP and Hans-Erwin PAULY

BOX PATENT APPLICATION

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1. Check for $1022.00
2. Transmittal Letter
3. Spec. 43 pgs. 4 indep. clms. and 31 clms. total
4. Drawings - 2 sheets of drawings containing 2 figures
5. Certified copy of German Application No. 100 64 827.4, filed December 22, 2000

Dated December 21, 2001

Docket No.: 05552.1450
CUSTOMER NUMBER: 22,852
EFC/FPD/peg Mail Drop 360

(Due Date: 12/22/01)

DK-TP
12-26-01

CPE 1SJH

PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

In Re Application of: Carsten SCHELP et al.

Serial No.: 10/024,258

Filed: December 21, 2001

For: DETECTION METHODS

Group Art Unit: Unknown

Examiner: Unknown

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1. Information Disclosure Statement
2. PTO-1449 form and 31 documents cited therein
3. Recordation Form Cover Sheet with executed Assignment
4. Check no. 059226 in the amount of $40.00 (recordation fee)

Dated: April 3, 2002

Docket No.: 05552.1450-00000 (Due Date: 03/21/02)

CPE/SJH/cob - MailDrop 216

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DKT'D 4-4-02 SJT